10/781,705>23/01/2007

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                E "375371-28-1"/BI,RN 25
L2              1 S E3 OR E5
                E "375371-23-6"/BI,RN 25
L3              1 S E3
                E "375371-22-5"/BI,RN 25
L4              1 S E3 OR E5
L5              2 S E7 OR E8
L6              3 S L1 OR L2 OR L3 OR L4 OR L5
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=> S E3 OR E5
             1 375371-22-5/BI
             1 375371-22-5P/BI
L4           1 375371-22-5/BI OR 375371-22-5P/BI

=> S E7 OR E8
             2 375371-24-7/BI
             1 375371-24-7P/BI
L5           2 375371-24-7/BI OR 375371-24-7P/BI

=> s l1 or l2 or l3 or l4 or l5
L6           3 L1 OR L2 OR L3 OR L4 OR L5

=> d l6 ibib abs hitstr 1-3

L6   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2003:836762  HCAPLUS
DOCUMENT NUMBER:          139:350474
TITLE:                    Preparation and compositions of nitrosothio
                          (hetero)cyclic nitric oxide donors
INVENTOR(S):              Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Lin,
                          Chia-en; Ranatunga, Ramani R.; Richardson, Stewart K.;
                          Wang, Tiansheng; Wang, Weiheng; Wey, Shiow-jyi
PATENT ASSIGNEE(S):       Nitromed, Inc., USA
SOURCE:                   PCT Int. Appl., 138 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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     WO 2003086282        A2    20031023    WO 2003-US10562          20030407
     WO 2003086282        A3    20040429
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2480832           A1    20031023    CA 2003-2480832          20030407
     AU 2003223491        A1    20031027    AU 2003-223491           20030407
     US 2003203915        A1    20031030    US 2003-407420           20030407
     EP 1497268           A2    20050119    EP 2003-719621           20030407
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2005537223        T     20051208    JP 2003-583309           20030407
PRIORITY APPLN. INFO.:                     US 2002-369873P      P   20020405
                                           WO 2003-US10562      W   20030407
OTHER SOURCE(S):          MARPAT 139:350474
GI
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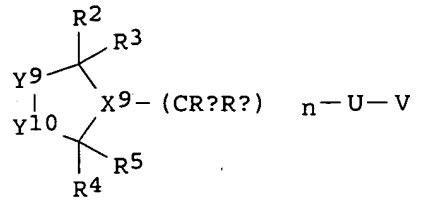

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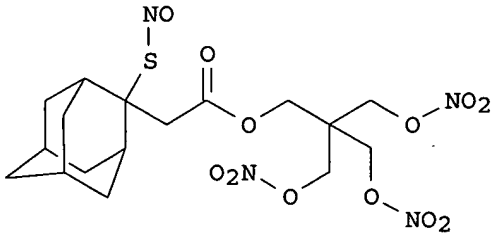
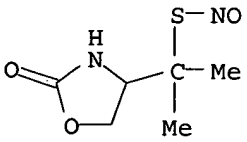


II

AB Title compds. I [wherein U = O, S, or NRaRi; V = NO or NO2; X9 = CR10 or N; Y9 = CR6R7, NRi, NR25, NRiCR6R7, CR6R7NRi, CR2R3CR6R7, or CR6R7CR2R3; Y10 = CR8R9 or CR8R9CR17R18; R2-R9, R17, and R18 = independently H or alkyl; or R2R3, R4R5, R6R7, or R8R9 = independently oxo; or R4 and R7 together with the C's to which they are attached = cycloalkyl; or CR6R7 = cycloalkyl; R6 and R9 taken together with the C's to which they are attached = (bridged)cycloalkyl, heterocyclyl, or aryl with the proviso that R7 and R8 are not present; R4 and R25 taken together with the C and N to which they are attached = heterocyclyl; Ra = lone pair of electrons, H, or (aryl)alkyl; Re and Rf = independently H, halo, OH, or (un)substituted (cyclo)alkyl, heterocyclyl, alkoxy, amino, aryl, etc.; or CReRf = heterocyclyl or (bridged) cycloalkyl; Ri = H or (un)substituted alkyl, aryl, carboxamido, sulfonamido, etc.; n = 0-3; and pharmaceutically acceptable salts thereof] were prepared as novel nitric oxide donors for use in compns. comprising at least one nitric oxide donor and optionally at least one therapeutic agent. The nitric oxide donors donate, transfer or release nitric oxide, and/or elevate endogenous levels of endothelium-derived relaxing factor, and/or stimulate endogenous synthesis of nitric oxide and/or are substrates for nitric oxide synthase and are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions (no data). For example, 2-[2-(nitrosothio)adamantan-2-yl]acetic acid was esterified with 3-nitrooxy-2,2-bis(nitrooxymethyl)propan-1-ol in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl and 4-dimethylaminopyridine in CH2Cl2 to give II (18%). The latter inhibited proliferation of human coronary artery smooth muscle cells with IC50 of 5 μM. In general, the nitrosylated compds. tested in this assay inhibited proliferation of vascular smooth muscle cells, while the corresponding non-nitrosylated derivs. showed no inhibition, slight inhibition, or exhibited much higher IC50 values. Thus, the invention provides methods for treating cardiovascular diseases, for the inhibition of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation, transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative, vascular diseases, for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis (no data). The invention also provides methods for treating inflammation, pain, fever, gastrointestinal disorders, respiratory disorders, and sexual dysfunctions (no data). In addition, the invention provides novel compns. and kits comprising at least one nitric oxide donor and/or at least one therapeutic agent.

IT 375371-24-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition component; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)
RN 375371-24-7 HCAPLUS
CN Thionitrous acid (HNOS), S-[1-methyl-1-(2-oxo-4-oxazolidinyl)ethyl] ester (9CI) (CA INDEX NAME)



L6 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:868945 HCAPLUS
DOCUMENT NUMBER: 136:575
TITLE: Infrared thermography and methods of use
INVENTOR(S): Marek, Przemyslaw A.; Trocha, Andzrej M.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001046471	A1	20011129	US 2001-850081	20010508
US 6762202 X NOOP	B2	20040713		
US 2004162243	A1	20040819	US 2004-781705	20040220

PRIORITY APPLN. INFO.: US 2000-202935P P 20000509
US 2001-850081 A1 20010508

OTHER SOURCE(S): MARPAT 136:575

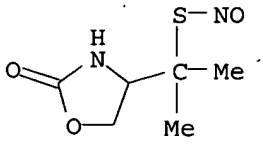
AB The present invention describes rapid noninvasive methods for measuring vasodilation or changes in blood flow in a patient following administration of at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one vasoactive agent. The method comprises the administration of at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one vasoactive agent to the patient followed by monitoring the temperature change of an area of interest using IR thermog. The present invention provides methods for diagnosing diseases or disorders related to vasodilation and changes in blood flow, such as, sexual dysfunction, Raynaud's syndrome, inflammation, hypertension, gastrointestinal disorders and central nervous system disorders. The sexual dysfunction is preferably female sexual dysfunction and female sexual arousal. The vasoactive agents include potassium channel activators, calcium channel blockers, α-adrenergic receptor antagonists, β-blockers, phosphodiesterase inhibitors, adenosine, ergot alkaloids, vasoactive intestinal peptides, prostaglandins, dopamine agonists, opioid antagonists, endothelin antagonists and thromboxane inhibitors. The present invention can also be used to screen and identify drug candidates for treating diseases, disorders and conditions resulting from

vasodilation or changes in blood flow. The present invention also describes compns. comprising at least one S-nitrosothiol compound for diagnosing, monitoring and/or treating female sexual dysfunctions.

IT 375371-24-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(IR thermog. for measuring vasodilation or changes in blood flow following administration of nitric oxide donor)

RN 375371-24-7 HCAPLUS

CN Thionitrous acid (HNOS), S-[1-methyl-1-(2-oxo-4-oxazolidinyl)ethyl] ester (9CI) (CA INDEX NAME)

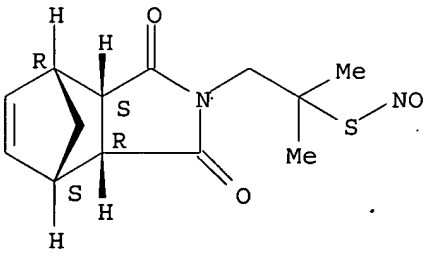


IT 375371-22-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(IR thermog. for measuring vasodilation or changes in blood flow following administration of nitric oxide donor)

RN 375371-22-5 HCAPLUS

CN Thionitrous acid (HNOS), S-[2-[(3aR,4S,7R,7aS)-1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-methano-2H-isoindol-2-yl]-1,1-dimethylethyl] ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

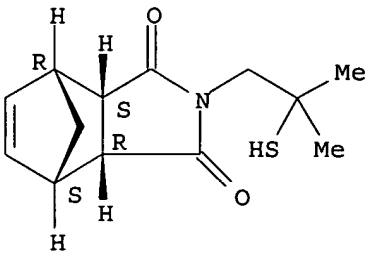


IT 375371-23-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(IR thermog. for measuring vasodilation or changes in blood flow following administration of nitric oxide donor)

RN 375371-23-6 HCAPLUS

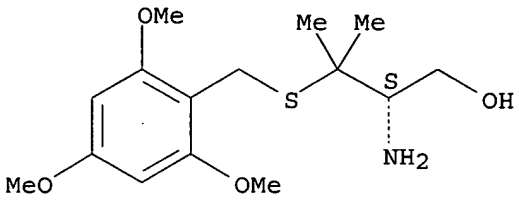
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 3a,4,7,7a-tetrahydro-2-(2-mercapto-2-methylpropyl)-, (3aR,4S,7R,7aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

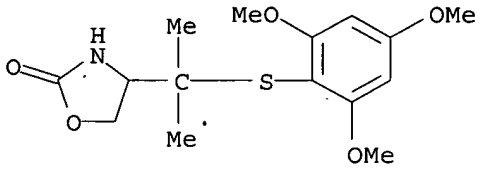


IT 364057-10-3P 375371-28-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(IR thermog. for measuring vasodilation or changes in blood flow following administration of nitric oxide donor)
RN 364057-10-3 HCAPLUS
CN 1-Butanol, 2-amino-3-methyl-3-[[(2,4,6-trimethoxyphenyl)methyl]thio]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 375371-28-1 HCAPLUS
CN 2-Oxazolidinone, 4-[1-methyl-1-[(2,4,6-trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:721438 HCAPLUS
DOCUMENT NUMBER: 135:288343
TITLE: Preparation and activity of nitrosated and nitrosylated nonsteroidal antiinflammatory compounds
INVENTOR(S): Bandarage, Upul K.; Dong, Qing; Fang, Xinqin; Garvey, David S.; Mercer, Gregory J.; Richardson, Stewart K.; Schroeder, Joseph D.; Wang, Tiansheng
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 182,433, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6297260 ← NO ODP	B1	20011002	US 1999-429019	19991029
CA 2348741	A1	20000511	CA 1999-2348741	19991029
WO 2000025776	A1	20000511	WO 1999-US25481	19991029
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1126838	A1	20010829	EP 1999-958708	19991029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528495	T	20020903	JP 2000-579217	19991029
AU 763000	B2	20030710	AU 2000-16012	19991029
US 2002016322	A1	20020207	US 2001-938560	20010827
US 6593347 ← NO ODP	B2	20030715		
US 2003207919	A1	20031106	US 2003-431457	20030508
AU 2004200091	A1	20040205	AU 2004-200091	20040109

PRIORITY APPLN. INFO.:	US 1998-182433	B2	19981030
	AU 2000-16012	A	19991029
	US 1999-429019	A3	19991029
	WO 1999-US25481	W	19991029
	US 2001-938560	A3	20010827

OTHER SOURCE(S): MARPAT 135:288343

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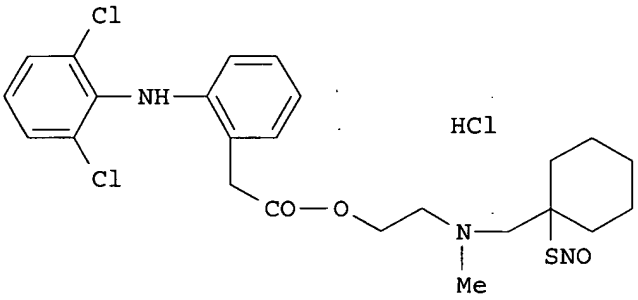


I

AB The present invention describes novel nitrosated and/or nitrosylated nonsteroidal antiinflammatory compds., and novel compns. comprising at least one nitrosated and/or nitrosylated nonsteroidal antiinflammatory compound, and, optionally, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase. The present invention also provides methods for treating, preventing and/or reducing inflammation, pain, and fever; decreasing or reversing the gastrointestinal, renal and other toxicities resulting from the use of nonsteroidal antiinflammatory drugs; treating and/or preventing gastrointestinal disorders; treating inflammatory disease states and disorders; and treating and/or preventing ophthalmic diseases or disorders. Thus, I was prepared in 8 steps from cyclohexanecarboxaldehyde and shows a relative activity of 1, 1.2 and 0.02 in analgesic, antiinflammatory and gastric lesion tests.

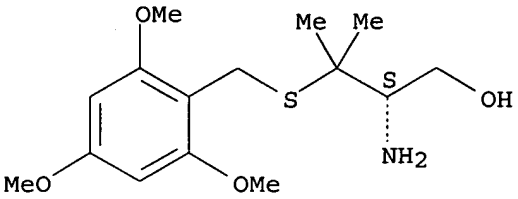
IT 364057-10-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and activity of nitrosated and nitrosylated nonsteroidal antiinflammatory compds.)

RN 364057-10-3 HCAPLUS

CN 1-Butanol, 2-amino-3-methyl-3-[[(2,4,6-trimethoxyphenyl)methyl]thio]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1050	"514/411".CCLS.	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:29
L2	73	l1 and (nitroso$)	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:29
L3	11	l2 and (tricyclo$)	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:29
L4	1124	"514/449".CCLS.	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:29
L5	139	l4 and (nitroso$)	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:29
L6	66	l5 and (oxazol$)	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:30
L7	23	l5 and (oxazolidin$)	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:30
S1	28	((STEWART) near2 (RICHARDSON)).INV.	US-PGPUB; USPAT	NEAR	ON	2006/09/20 17:04
S2	2	("6762202").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/06 16:02
S3	3	((PRZEMYSLAW) near2 (MAREK)).INV.	US-PGPUB; USPAT	NEAR	ON	2007/01/23 19:11
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S5	113	((wang) near2 (peng)).INV.	US-PGPUB; USPAT	NEAR	ON	2006/09/08 12:49
S6	1	S4 and S5	US-PGPUB; USPAT	NEAR	ON	2006/09/08 12:49
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S8	76	"514/515".CCLS.	US-PGPUB; USPAT	NEAR	ON	2006/09/18 13:06
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S10	2	("6193992").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/18 13:40
S11	380	"424/430".CCLS.	US-PGPUB; USPAT	NEAR	ON	2006/09/18 13:40

EAST Search History

S12	142	S11 and sex$	US-PGPUB; USPAT	NEAR	ON	2006/09/18 13:41
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S14	29	S11 and nitric	US-PGPUB; USPAT	NEAR	ON	2006/09/18 13:42
S15	10	S14 and S12	US-PGPUB; USPAT	NEAR	ON	2006/09/18 13:42
S16	0	nitroso NEAR5 sex$	US-PGPUB; USPAT	NEAR	ON	2006/09/20 17:04
S17	1	nitroso NEAR10 sex$	US-PGPUB; USPAT	NEAR	ON	2006/09/20 17:42
S20	11	nitrite NEAR10 sex$	US-PGPUB; USPAT	NEAR	ON	2006/09/20 17:43
S21	1	nitroso NEAR15 sex$	US-PGPUB; USPAT	NEAR	ON	2007/01/23 18:26
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S24	3	((PRZEMYSLAW) near2 (MAREK)).INV.	US-PGPUB; USPAT	NEAR	ON	2007/01/23 19:07
S25	77	"514/515".CCLS.	US-PGPUB; USPAT	NEAR	ON	2007/01/23 19:07
S26	383	"424/430".CCLS.	US-PGPUB; USPAT	NEAR	ON	2007/01/23 20:27
S27	3	S26 and nitroso	US-PGPUB; USPAT	NEAR	ON	2007/01/23 19:07
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S30	29	S26 and nitric	US-PGPUB; USPAT	NEAR	ON	2007/01/23 19:07
S31	45	"6297260"	US-PGPUB; USPAT	NEAR	ON	2007/01/23 19:11
S32	2	("6297260").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/01/23 19:11